## SEQUENCE LISTING

<110> POELLINGER, Lorenz

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RUAS, Jorge

<120> MECHANISM OF CONDITIONAL REGULATION OF THE HYPOXIA-INDUCIBLE
FACTOR-1 BY THE VON HIPPEL-LINDAU TUMOR SUPPRESSOR PROTEIN

<130> 3743/49008

<150> US 60/223,480

<151> 2000-08-07

<160> 7

<170> PatentIn version 3.0

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ggc gcc gag gag gag atg gag gcc ggg ccg ccg ccg ccc gtg ctg cgc cg Gly Ala Glu Glu Met Glu Ala Gly Arg Pro Arg Pro Val Leu Arg 50 55 60

tcg gtg aac Ser Val Asn 65					le Phe				240
ccg cgc gtc Pro Arg Val									288
ccc tac cca Pro Tyr Pro		-			-	Ile H			336
cga ggt cac Arg Gly His 115									384
ctg gtt aac Leu Val Asn 130									432
cag cct att Gln Pro Ile 145	_		_	Pro Va	-		-		480
cga tgc ctc Arg Cys Leu									528
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caa cgg atg Gln Arg Met 210		tga							642
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Ser Gly Ala 35	Glu Glu	Ser Gly	Pro Glu 40	Glu Se	er Gly	Pro G	lu Glu	Leu	

Gly Ala Glu Glu Met Glu Ala Gly Arg Pro Arg Pro Val Leu Arg 50 60

Ser Val Asn Ser Arg Glu Pro Ser Gln Val Ile Phe Cys Asn Arg Ser 65 70 75 80

Pro Arg Val Val Leu Pro Val Trp Leu Asn Phe Asp Gly Glu Pro Gln 85 90 95

Pro Tyr Pro Thr Leu Pro Pro Gly Thr Gly Arg Arg Ile His Ser Tyr 100 105 110

Arg Gly His Leu Trp Leu Phe Arg Asp Ala Gly Thr His Asp Gly Leu 115 120 125

Gln Pro Ile Phe Ala Asn Ile Thr Leu Pro Val Tyr Thr Leu Lys Glu 145 150 155 160

Arg Cys Leu Gln Val Val Arg Ser Leu Val Lys Pro Glu Asn Tyr Arg 165 170 175

Arg Leu Asp Ile Val Arg Ser Leu Tyr Glu Asp Leu Glu Asp His Pro 180 185 190

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	cga Arg															96
	tct Ser															144
	gtg Val 50															192
agc Ser 65	tat Tyr	ttg Leu	cgt Arg	gtg Val	agg Arg 70	aaa Lys	ctt Leu	ctg Leu	gat Asp	gct Ala 75	ggt Gly	gat Asp	ttg Leu	gat Asp	att Ile 80	240
	gat Asp															288
	ggt Gly															336
	gat Asp															384
	cac His 130															432
	gaa Glu															480
	aac Asn		~	-	_				_	_	-	_				528
agc Ser	cga Arg	gga Gly	aga Arg 180	act Thr	atg Met	aac Asn	ata Ile	aag• Lys 185	tct Ser	gca Ala	aca Thr	tgg Trp	aag Lys 190	gta Val	ttg Leu	576
	tgc Cys															624
	tgt Cys 210															672
-	ccc Pro								-				-	_	-	720
	ttc Phe															768

250 255 245 816 gaa aga att acc gaa ttg atg gga tat gag cca gaa gaa ctt tta ggc Glu Arg Ile Thr Glu Leu Met Gly Tyr Glu Pro Glu Glu Leu Leu Gly 265 260 864 cgc tca att tat gaa tat tat cat gct ttg gac tct gat cat ctg acc Arg Ser Ile Tyr Glu Tyr Tyr His Ala Leu Asp Ser Asp His Leu Thr 280 aaa act cat cat gat atg ttt act aaa gga caa gtc acc aca gga cag 912 Lys Thr His His Asp Met Phe Thr Lys Gly Gln Val Thr Thr Gly Gln 290 295 300 960 tac agg atg ctt gcc aaa aga ggt gga tat gtc tgg gtt gaa act caa Tyr Arg Met Leu Ala Lys Arg Gly Gly Tyr Val Trp Val Glu Thr Gln 310 305 1008 qca act qtc ata tat aac acc aag aat tct caa cca cag tgc att gta Ala Thr Val Ile Tyr Asn Thr Lys Asn Ser Gln Pro Gln Cys Ile Val 330 1056 tgt gtg aat tac gtt gtg agt ggt att att cag cac gac ttg att ttc Cys Val Asn Tyr Val Val Ser Gly Ile Ile Gln His Asp Leu Ile Phe 340 345 1104 tcc ctt caa caa aca gaa tgt gtc ctt aaa ccg gtt gaa tct tca gat Ser Leu Gln Gln Thr Glu Cys Val Leu Lys Pro Val Glu Ser Ser Asp 360 1152 atg aaa atg act cag cta ttc acc aaa gtt gaa tca gaa gat aca agt Met Lys Met Thr Gln Leu Phe Thr Lys Val Glu Ser Glu Asp Thr Ser 375 1200 age etc ttt gae aaa ett aag aag gaa eet gat get tta aet ttg etg Ser Leu Phe Asp Lys Leu Lys Lys Glu Pro Asp Ala Leu Thr Leu Leu 390 gee eca gee get gga gae aca ate ata tet tta gat ttt gge age aac 1248 Ala Pro Ala Ala Gly Asp Thr Ile Ile Ser Leu Asp Phe Gly Ser Asn 405 410 1296 gac aca gaa act gat gac cag caa ctt gag gaa gta cca tta tat aat Asp Thr Glu Thr Asp Asp Gln Gln Leu Glu Glu Val Pro Leu Tyr Asn 420 430 gat gta atg ctc ccc tca ccc aac gaa aaa tta cag aat ata aat ttg 1344 Asp Val Met Leu Pro Ser Pro Asn Glu Lys Leu Gln Asn Ile Asn Leu 435 1392 gca atg tct cca tta ccc acc gct gaa acg cca aag cca ctt cga agt Ala Met Ser Pro Leu Pro Thr Ala Glu Thr Pro Lys Pro Leu Arg Ser 450 455 agt gct gac cct gca ctc aat caa gaa gtt gca tta aaa tta gaa cca 1440 Ser Ala Asp Pro Ala Leu Asn Gln Glu Val Ala Leu Lys Leu Glu Pro 465 aat cca gag tca ctg gaa ctt tct ttt acc atg ccc cag att cag gat 1488 Asn Pro Glu Ser Leu Glu Leu Ser Phe Thr Met Pro Gln Ile Gln Asp 490

Page 5

1536

cag aca cct agt cct tcc gat gga agc act aga caa agt tca cct gag

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cct Pro	aat Asn	agt Ser 515	ccc Pro	agt Ser	gaa Glu	tat Tyr	tgt Cys 520	ttt Phe	tat Tyr	gtg Val	gat Asp	agt Ser 525	gat Asp	atg Met	gtc Val	1584
aat Asn	gaa Glu 530	ttc Phe	aag Lys	ttg Leu	gaa Glu	ttg Leu 535	gta Val	gaa Glu	aaa Lys	ctt Leu	ttt Phe 540	gct Ala	gaa Glu	gac Asp	aca Thr	1632
gaa Glu 545	gca Ala	aag Lys	aac Asn	cca Pro	ttt Phe 550	tct Ser	act Thr	cag Gln	gac Asp	aca Thr 555	gat Asp	tta Leu	gac Asp	ttg Leu	gag Glu 560	1680
atg Met	tta Leu	gct Ala	ccc Pro	tat Tyr 565	atc Ile	cca Pro	atg Met	gat Asp	gat Asp 570	gac Asp	ttc Phe	cag Gln	tta Leu	cgt Arg 575	tcc Ser	1728
ttc Phe	gat Asp	cag Gln	ttg Leu 580	tca Ser	cca Pro	tta Leu	gaa Glu	agc Ser 585	agt Ser	tcc Ser	gca Ala	agc Ser	cct Pro 590	gaa Glu	agc Ser	1776
gca Ala	agt Ser	cct Pro 595	caa Gln	agc Ser	aca Thr	gtt Val	aca Thr 600	gta Val	ttc Phe	cag Gln	cag Gln	act Thr 605	caa Gln	ata Ile	caa Gln	1824
gaa Glu	cct Pro 610	act Thr	gct Ala	aat Asn	gcc Ala	acc Thr 615	act Thr	acc Thr	act Thr	gcc Ala	acc Thr 620	act Thr	gat Asp	gaa Glu	tta Leu	1872
aaa Lys 625	aca Thr	gtg Val	aca Thr	aaa Lys	gac Asp 630	cgt Arg	atg Met	gaa Glu	gac Asp	att Ile 635	aaa Lys	ata Ile	ttg Leu	att Ile	gca Ala 640	1920
tct Ser	cca Pro	tct Ser	cct Pro	acc Thr 645	His	ata Ile	cat His	aaa Lys	gaa Glu 650	Thr	act Thr	agt Ser	gcc Ala	aca Thr 655	tca Ser	1968
tca Ser	cca Pro	tat Tyr	aga Arg 660	Asp	act Thr	caa Gln	agt Ser	cgg Arg 665	Thr	gcc Ala	tca Ser	cca Pro	aac Asn 670	Arg	gca Ala	2016
gga Gly	aaa Lys	gga Gly 675	. Val	ata Ile	gaa Glu	cag Gln	aca Thr 680	Glu	aaa Lys	tct Ser	cat His	cca Pro 685	Arg	agc Ser	cct Pro	2064
Asn	Val 690	Leu	. Ser	· Val	. Ala	Leu 695	. Ser	Gln	a Arg	, Thr	700	) Val	. Pro	GIU	ggaa 1 Glu	2112
gaa Glu 705	Leu	aat Asn	cca Pro	aag Lys	ata Ile 710	Leu	gct Ala	tto Lev	g caç ı Glr	aat Asr 715	n Ala	caç a Glr	g aga n Arg	ı aaç J Lys	g cga S Arg 720	2160
Lys	: Met	: Glu	ı His	725	Gly	Ser	: Leu	ı Phe	e Glr 730	n Ala )	a Val	l Gly	/ I16	735		2208
tta Leu	tta Leu	ı caç ı Glr	g cac n Glr 740	n Pro	a gad Asp	gat Asp	cat His	gca Ala 745	a Ala	act Thi	aca Thi	a tca r Sei	t ctt Lei 750	ı Sei	tgg Trp	2256

				tgc Cys										2304
~				ata Ile		_		_	_	_	_		~ ~ ~	2352
	_	_	~	agt Ser 790			_	_		_		_	-	2400
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Arg Arg Lys Glu Lys Ser Arg Asp Ala Ala Arg Ser Arg Arg Ser Lys 20 25 30

Glu Ser Glu Val Phe Tyr Glu Leu Ala His Gln Leu Pro Leu Pro His 35 40 45

Asn Val Ser Ser His Leu Asp Lys Ala Ser Val Met Arg Leu Thr Ile  $50 \hspace{1.5cm} 55 \hspace{1.5cm} 60$ 

Ser Tyr Leu Arg Val Arg Lys Leu Leu Asp Ala Gly Asp Leu Asp Ile 65 70 75 80

Glu Asp Asp Met Lys Ala Gln Met Asn Cys Phe Tyr Leu Lys Ala Leu 85 90 95

Asp Gly Phe Val Met Val Leu Thr Asp Asp Gly Asp Met Ile Tyr Ile 100 105 110

Ser Asp Asn Val Asn Lys Tyr Met Gly Leu Thr Gln Phe Glu Leu Thr 115 120 125

z 1 1

Gly His Ser Val Phe Asp Phe Thr His Pro Cys Asp His Glu Glu Met 130 135 Arg Glu Met Leu Thr His Arg Asn Gly Leu Val Lys Lys Gly Lys Glu Gln Asn Thr Gln Arg Ser Phe Phe Leu Arg Met Lys Cys Thr Leu Thr 170 165 Ser Arg Gly Arg Thr Met Asn Ile Lys Ser Ala Thr Trp Lys Val Leu His Cys Thr Gly His Ile His Val Tyr Asp Thr Asn Ser Asn Gln Pro 200 Gln Cys Gly Tyr Lys Lys Pro Pro Met Thr Cys Leu Val Leu Ile Cys Glu Pro Ile Pro His Pro Ser Asn Ile Glu Ile Pro Leu Asp Ser Lys 230 235 Thr Phe Leu Ser Arg His Ser Leu Asp Met Lys Phe Ser Tyr Cys Asp Glu Arg Ile Thr Glu Leu Met Gly Tyr Glu Pro Glu Glu Leu Leu Gly 265 Arg Ser Ile Tyr Glu Tyr Tyr His Ala Leu Asp Ser Asp His Leu Thr Lys Thr His His Asp Met Phe Thr Lys Gly Gln Val Thr Thr Gly Gln 295 290 Tyr Arg Met Leu Ala Lys Arg Gly Gly Tyr Val Trp Val Glu Thr Gln Ala Thr Val Ile Tyr Asn Thr Lys Asn Ser Gln Pro Gln Cys Ile Val Cys Val Asn Tyr Val Val Ser Gly Ile Ile Gln His Asp Leu Ile Phe Ser Leu Gln Gln Thr Glu Cys Val Leu Lys Pro Val Glu Ser Ser Asp

Met Lys Met Thr Gln Leu Phe Thr Lys Val Glu Ser Glu Asp Thr Ser

375

Ser Leu Phe Asp Lys Leu Lys Lys Glu Pro Asp Ala Leu Thr Leu Leu 390 395 Ala Pro Ala Ala Gly Asp Thr Ile Ile Ser Leu Asp Phe Gly Ser Asn Asp Thr Glu Thr Asp Asp Gln Gln Leu Glu Glu Val Pro Leu Tyr Asn Asp Val Met Leu Pro Ser Pro Asn Glu Lys Leu Gln Asn Ile Asn Leu 440 Ala Met Ser Pro Leu Pro Thr Ala Glu Thr Pro Lys Pro Leu Arg Ser 450 455 Ser Ala Asp Pro Ala Leu Asn Gln Glu Val Ala Leu Lys Leu Glu Pro 470 Asn Pro Glu Ser Leu Glu Leu Ser Phe Thr Met Pro Gln Ile Gln Asp 485 490 Gln Thr Pro Ser Pro Ser Asp Gly Ser Thr Arg Gln Ser Ser Pro Glu Pro Asn Ser Pro Ser Glu Tyr Cys Phe Tyr Val Asp Ser Asp Met Val 520 Asn Glu Phe Lys Leu Glu Leu Val Glu Lys Leu Phe Ala Glu Asp Thr Glu Ala Lys Asn Pro Phe Ser Thr Gln Asp Thr Asp Leu Asp Leu Glu 545 Met Leu Ala Pro Tyr Ile Pro Met Asp Asp Phe Gln Leu Arg Ser 565 570 Phe Asp Gln Leu Ser Pro Leu Glu Ser Ser Ser Ala Ser Pro Glu Ser Ala Ser Pro Gln Ser Thr Val Thr Val Phe Gln Gln Thr Gln Ile Gln 595 600 605 Glu Pro Thr Ala Asn Ala Thr Thr Thr Thr Ala Thr Thr Asp Glu Leu Lys Thr Val Thr Lys Asp Arg Met Glu Asp Ile Lys Ile Leu Ile Ala

Ser Pro Ser Pro Thr His Ile His Lys Glu Thr Thr Ser Ala Thr Ser 645 650 655

Ser Pro Tyr Arg Asp Thr Gln Ser Arg Thr Ala Ser Pro Asn Arg Ala 660 665 670

Gly Lys Gly Val Ile Glu Gln Thr Glu Lys Ser His Pro Arg Ser Pro 675 680 685

Asn Val Leu Ser Val Ala Leu Ser Gln Arg Thr Thr Val Pro Glu Glu 690 695 700

Lys Met Glu His Asp Gly Ser Leu Phe Gln Ala Val Gly Ile Gly Thr  $725 \ 730 \ 735$ 

Leu Leu Gln Gln Pro Asp Asp His Ala Ala Thr Thr Ser Leu Ser Trp  $740 \hspace{1.5cm} 745 \hspace{1.5cm} 750$ 

Lys Arg Val Lys Gly Cys Lys Ser Ser Glu Gln As<br/>n Gly Met Glu Gln 755 760 765

Lys Thr Ile Ile Leu Ile Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly 770 775 780

Gln Ser Met Asp Glu Ser Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys 785 790 795 800

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Glu Leu Leu Arg Ala Leu Asp Gln Val Asn 820 825

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4 1 9 8

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